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1. A method of treating or preventing cancer, cardiovascular disease, Down's syndrome, or neural tube defects in a subject, said method comprising inhibiting methionine synthase reductase biological activity in said subject.

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2. A method of treating or preventing cardiovascular disease or Down's Syndrome, said method comprising administering to the subject to a therapeutically effective dose of a metabolite or cofactor selected from the group: folate, cobalamin, S-adenosyl methionine, betaine, or methionine.

3. The method of claim 1 or 2, wherein said subject has been diagnosed as having a mutation or polymorphism in methionine synthase reductase.

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4. A method of preventing neural tube defects, cancer, cardiovascular disease, or Down's Syndrome, said method comprising:

a) detecting an increased risk of neural tube defects, cancer, cardiovascular disease, or Down's Syndrome wherein said detecting is by analyzing methionine synthase reductase nucleic acid from one or more test subjects selected from: a mammal; a potential parent, either male or female; a pregnant mammal; or a developing embryo or fetus, wherein said analyzing is done by the method of claim D; and

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b) exposing said mammal, said potential parent, said pregnant mammal, and/or said developing embryo or fetus to a therapeutically effective dose of a metabolite or cofactor selected from the group: cobalamin; S-adenosyl methionine; betaine; or methionine, wherein said exposing is via the administration of said

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dose to said mammal, said potential parent, said ~~pregnant mammal~~, and/or said developing embryo or fetus.

546 B² 5. The method of claim 1, 2, or 4, wherein said cardiovascular disease is premature coronary artery disease.

5 6. A method for detecting an increased risk of developing a neural tube defect, Down's Syndrome, or cardiovascular disease in a mammalian embryo or fetus, said method comprising detecting the presence of a polymorphic methionine synthase reductase (MTRR) in a test subject, wherein said test subject is a future parent of said embryo or said fetus, and wherein detection of a homozygous
10 MTRR polymorphism in said future parent, said embryo, or said fetus, or detection of either a homozygous or heterozygous MTRR polymorphism in both future parents, indicates an increased risk of developing said neural tube defect in said embryo or said fetus.

15 7. The method of claim 6, wherein said polymorphic MTRR is detected by analyzing nucleic acid from said test subject.

8. The method of claim 7, wherein said nucleic acid is genomic DNA.

9. The method of claim 7, wherein said nucleic acid is cDNA.

10. The method of claim 7, wherein said nucleic acid contains a G

instead of an A at the third position of the twenty-second codon (nucleotide position 66, relative to the first nucleotide of the start codon) of MTRR.

11. The method of claim 7, said method further comprising:

- a) PCR-amplifying a segment of MTRR nucleic acid using
5 primers MSG108S (SEQ ID NO: 49) and AD292 (SEQ ID NO: 50), and
- b) digesting the product of the PCR amplification reaction with the restriction enzyme *Nde* I, wherein a PCR product that is digested by *Nde* I indicates an increased risk of developing a neural tube defect in a mammalian embryo or fetus.

10 12. The method of claim 6, wherein said polymorphic MTRR is detected by analyzing MTRR polypeptide from said test subject.

13. The method of claim 6, wherein said test subject is a future female parent of said embryo or said fetus.

15 14. The method of claim 6, wherein said test subject is said embryo or said fetus.

15. The method of claim 6, said method further comprising detecting the presence of a polymorphic methylenetetrahydrofolate reductase (MTHFR) in a test subject, wherein detection of said polymorphic MTHFR indicates an increased risk of developing said neural tube defect, Down's Syndrome, or cardiovascular

disease in said embryo or said fetus.

16. The method of claim 15, wherein said polymorphic MTHFR has a T instead of a C at a nucleotide position equivalent to position 677 of SEQ ID NO: 51.

5 17. The method of claim 15, wherein said polymorphic MTHFR is detected by analyzing nucleic acid from said test subject.

18. The method of claim 15, wherein said polymorphic MTHFR is detected by analyzing polypeptide from said test subject.

10 19. The method of claim 6, said method further comprising measuring the level of cobalamin in said test subject, wherein a low cobalamin level indicates an increased risk of developing said neural tube, cardiovascular disease or Down's Syndrome defect in said embryo or said fetus.

20. The method of claim 6, wherein said polymorphic MTRR contains a methionine instead of an isoleucine at amino acid position 22.

15 21. The method of claim 6, wherein said cardiovascular disease is premature coronary artery disease.

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